12-06-2024

To: ADRDSummit2025@ninds.nih.gov

Delivered Electronically

Re: ADRD Summit RFI

The genetic ALS & FTD community is thankful for the committed dedication of the NIH, many academic researchers, industry, non-profit organizations, and people with lived experience of Alzheimer's Related Dementias that helped develop the 2022 report on ADRD Research priorities. Founded in 2023, we are proud to be the first organization dedicated exclusively to the interests of the genetic ALS & FTD community and are pleased to have this chance to share our communities perspective on this important topic.

First, we must call for ever greater coordination of research for the linked diseases of ALS and FTD, and all TDP-43 and Tau linked diseases. It is unconscionable that scientific discoveries linked to all of these diseases based on shared characteristics would only help one of them. We can see in the history of the divided therapeutic management of C9orf72 ALS vs FTD despite the animal and cellular models of these two variations being one and the same.

Secondly, while we all share a passionate drive to understand the earliest signs of these diseases we must ensure that harm does not befall those altruistically participating in research. The turning of a loved one of a healthy person into a behavioral informant is a prima facie risk to what should be relationships centered on trust for the perspectives of both parties. This risk has never been investigated, nor is it communicated in the informed consent process to individuals asked to undergo this surveillance. This is related to the stigmatization of presymptomatic genetic communities with broad and deterministic language that uses harsh and demeaning language to describe minor and functionally

imperceptible differences in cognitive tests. Our communities of those impacted by genetic ALS and FTD should not be disadvantaged or harmed by the research seeking the prevention of ALS and FTD.

Thirdly, the categorization of the presymptomatic period should be focused on biological measures. We do not call for a full ban on presymptomatic cognitive exploration with it's possibility to provide insights into disease pathogenesis , but we must stress it will never be practical or tolerable to institute lifelong cognitive surveillance of those at risk in clinical application of prevention. Biological measures carry little of the stigma or stress related to the questioning of one's cognitive abilities especially prior to any subjective complaints.

Finally, regarding new research that we have been a part of that should be considered, we point you to the recently published review article "Guidance for Clinical Management of Pathogenic Variant Carriers at Elevated Genetic Risk of ALS / FTD"- https://jnnp.bmj.com/content/early/2024/11/18/jnnp-2024-334339 . Genetic ALS & FTD: End the Legacy co-sponsored and played a substantial role in the workshop from which the article was derived, and I was a contributing author. This document for the first time established concrete advice on what to do and consider as a person at risk.

In appreciation of all working to end these diseases,

Jean Swidler

Genetic ALS & FTD: End the Legacy

EndTheLegacy.org